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THE SOCIETY FOR LIFE SCIENCE PROFESSIONALS

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From the Office of the President and CEO

7 JUL 8 AM 7:38

6 July 2004

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Dear Sir/Madam:

We are pleased to submit the attached ISPE GAMP response to the FDA Part 11 revisions. Our response includes a general comment letter which refers to two presentations (attached) which were due to be delivered at the cancelled public meeting. We will follow up this Email with a hard copy submission via next day courier.

Thank you for making our response part of the record. If you have any questions please contact me at (813) 960-2105.

Sincerely,

Robert P. Best

Robert P. Best
President/CEO

RPB/dwm

Attachments

INDIVIDUALS
ACADEMIA ISPE INDUSTRY
GOVERNMENT

2004N-0133

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Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

RE: "Electronic Records; Electronic Signatures; Public Meeting"
Docket No. 2004N-0133

Dear Sir/Madam:

ISPE welcomes the opportunity to submit comments in response to FDA questions concerning Part 11. ISPE is an international society promoting the integration of industry professionals and regulatory agencies worldwide to improve the Life Sciences.

The ISPE technical sub-committee known as GAMP Forum has prepared the comments submitted here. GAMP Forum is an international organization with active regional steering committees for USA, Europe, and Japan. Membership includes pharmaceutical companies, suppliers, and consultants. The GAMP Forum is responsible for the GAMP4 Guide and is currently working on new Electronic Record/Signature Guidance.

ISPE/GAMP appreciate the difficulty the Agency has in being completely definitive in this area but believe that the following comments will make the Rule more effective. In particular we believe the proposed changes will help facilitate new technology and innovation (e.g. PAT). Although our comments are largely based on a pharmaceutical sector we believe the points made here are equally applicable to the other sectors subject to Part 11.

1) We suggest the Part 11 Rule should be aligned with FDA's Part 11 Final Guidance on Scope and Application issued August 2003. In particular, we encourage the Agency to:
   - Preserve and clarify narrow scope
   - Focus on signatures and records, not data and systems
   - Emphasize role of predicate rules

2) The Rule should allow the application and rigor of <u>all controls</u> (not just audit trail, validation, and record retention) to be based on impact and risk. It should be a decision of the regulated organization whether or not they wish to apply a risk-based approach. If a risk-based approach is applied then it should be defined and documented by the regulated organization.

3) We suggest that there should be a general expectation that computer systems supporting regulated records and signatures are validated. Not all Predicate Rules clearly identify a requirement for such validation. Any such validation should be commensurate with impact and risk.

4) Part 11 should concentrate on the *principles of what* is needed and avoid being prescriptive on the *practicalities of how* to fulfill Part 11 Rule. For instance, for electronic signatures there should be controls in place to ensure that only the actual (verified) owner of the electronic signature could perform actions recorded against that electronic signature. We suggest that 11.200(a) (3) is replaced with "Electronic signatures must be administered to ensure that attempted use of an individual's electronic signature by anyone other than its genuine owner is appropriately controlled."

5) We would like to suggest that the preamble to any Part 11 revision is kept as short as possible. If further interpretation is necessary, it should be published as separate guidance and not as part of the preamble. This will allow the Rule to be less prescriptive and, therefore, give it a 'longer life'. It would be very useful if any such additional guidance is released in conjunction with publication of the revised Rule.

6) The current Part 11 Rule should be maintained with the accompanying Part 11 Final Guidance on Scope and Application until any revision to the Rule is issued. We believe rescinding Part 11 without replacement would lead to a period of ambiguity until the Agency published their revised requirements.

In addition to these comments, please find attached the two presentations for your consideration that ISPE/GAMP was to have made at the Agency's planned Public Meeting on Part 11 Rulemaking originally planned for 11 June 2004, but cancelled because of President Regan's funeral.

Thank you for the opportunity to comment.

Yours Sincerely,

Bob Best

Attachment #1: GAMP Forum Part 11 Comments
Attachment #2: New ISPE/GAMP Guidance on Compliant Electronic Records and Signatures

THE SOCIETY FOR
LIFE SCIENCE PROFESSIONALS

Part 11 Comments

Dr Guy Wingate
Chairman - GAMP Council
guy.wingate@gsk.com

GAMP Forum

- Technical Sub-Committee of ISPE
- GAMP Forum is international organisation with active regional steering committees for USA, Europe, and Japan
- Membership includes pharmaceutical companies, suppliers, consultants and regulators
- Responsible for GAMP4 Guide and working on new Electronic Record/Signature Guidance

Scope of Presentation

- Part 11 applies to all FDA regulated industries
- This presentation is largely based on a pharmaceutical sector perspective
- We believe the points made here are equally applicable to the other sectors

Top Recommendations

1) Align the Rule with the intent of FDA's Part 11 Final Guidance on Scope and Application
   - Preserve and clarify narrow scope
   - Focus on signatures and records, not systems or data
   - Emphasize predicate rules
2) Application and rigor for all controls can be based on impact and risk
3) Computer systems validation expected but commensurate with impact

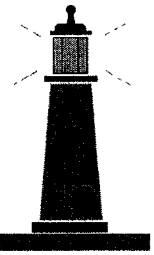
Potential Part 11 Rulemaking

- Part 11 Rule should concentrate on *what* is needed and avoid being prescriptive on *how* to fulfil Part 11 Rule
- If risk based approach is used then it should be defined and documented by user organisation
- Keep new preamble to any Part 11 revision short. If additional guidance is needed then should be made as separate guidance document

New GAMP Good Practice Guide for Electronic Record and Signature Compliance

Arthur D. Perez, Ph.D.
Chairman, GAMP Americas

Guiding Principles for New GPG



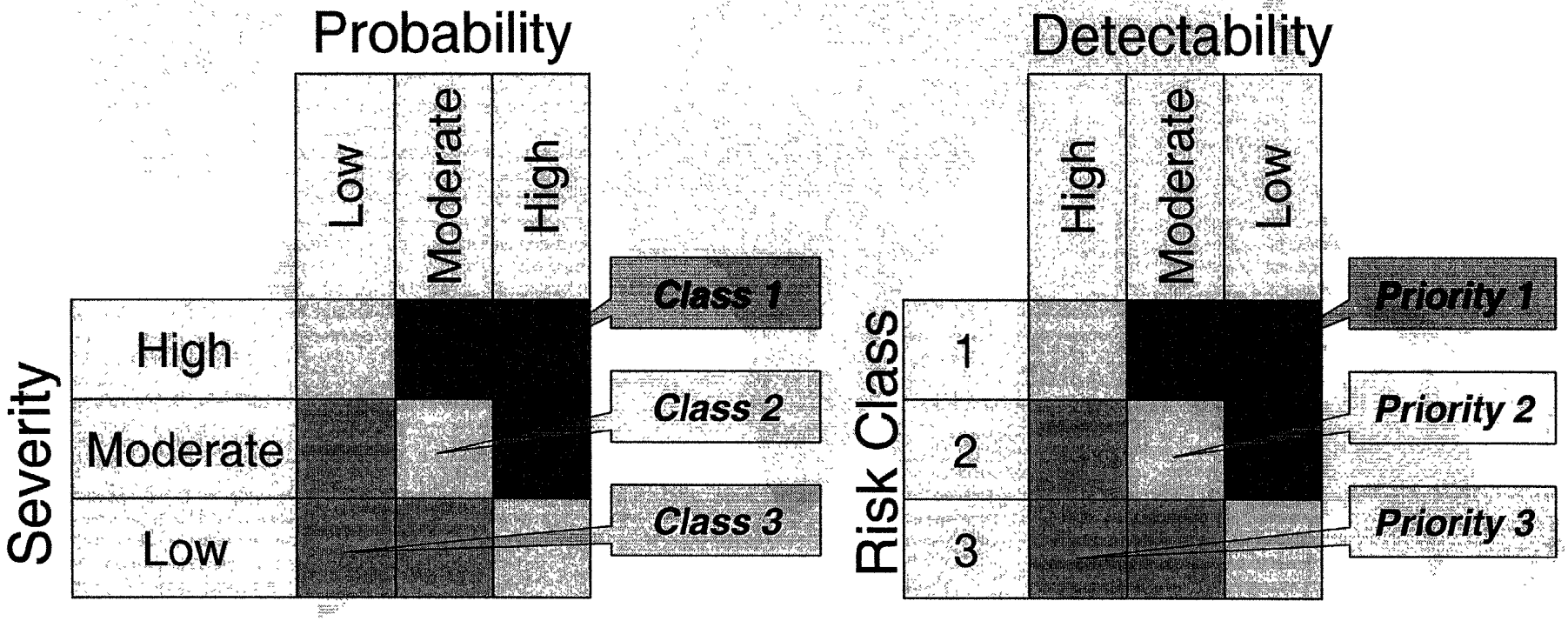
- Consistent approach to ERS management
- Manage risk by
  - Defining minimal acceptable standards
  - Applying stronger measures only where warranted
- Simplicity of Approach
  - Assessment must not be harder than applying maximum controls
- Facilitate interpretation of predicate rule requirements
- Minimal impact on transition from old compliance programs to new
- Encourage and facilitate new technologies that may involve electronic records and/or signatures
- Consider and comply with international regulations
  - Including USFDA, EU, PIC/S Guidance, Japanese MHLW

Key Concepts

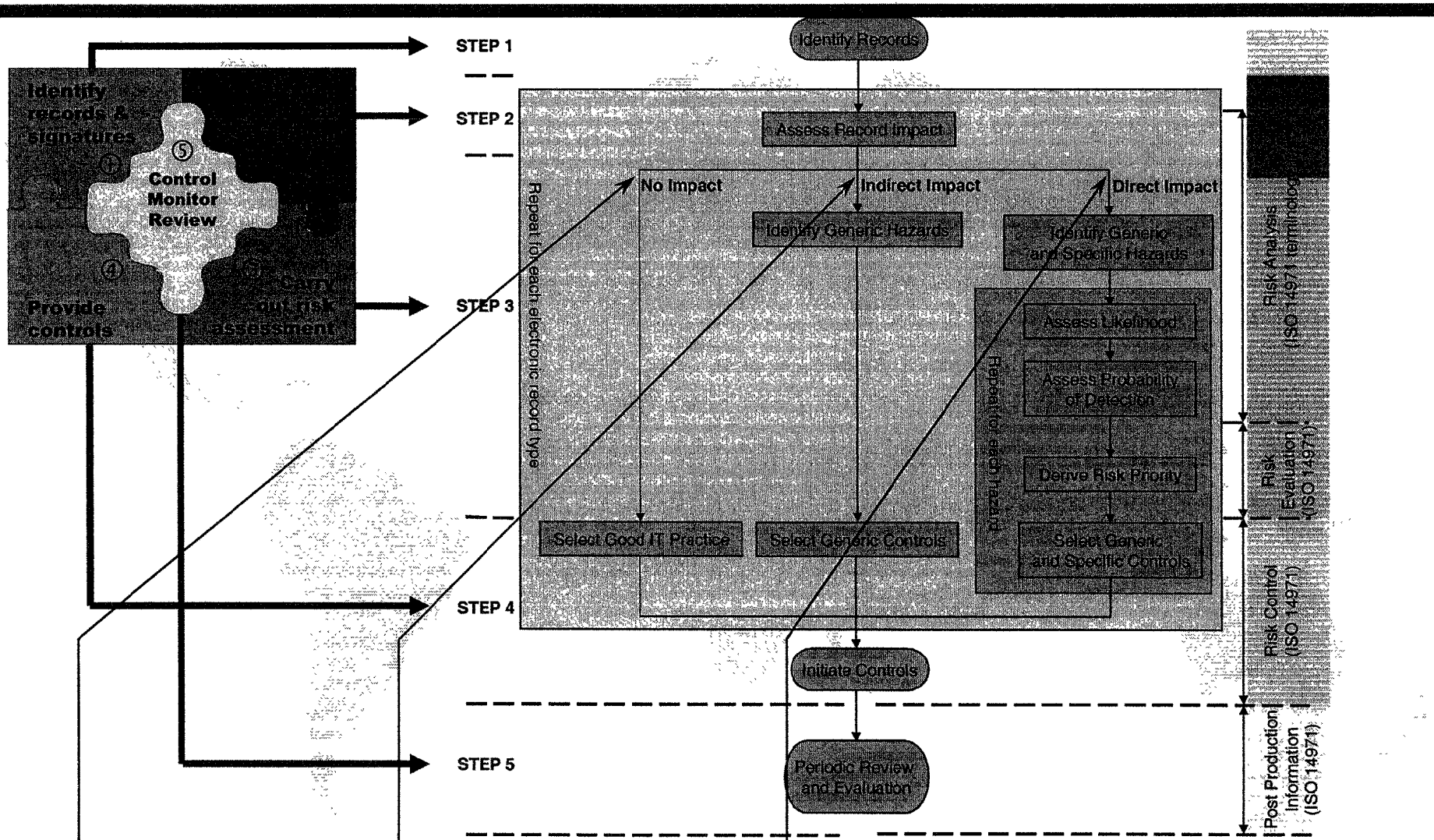
- Scalability of assessment process based on *record impact*
  - **Direct Impact** records have obvious and significant effect on public health
  - **Indirect Impact** records that provide evidence of compliance but do not have obvious and significant effect on public health
  - **Non-impact** records that have negligible or no effect on public health
- Identify the potential hazards
  - Possible occurrences that could threaten a record
    - Power failure, security breach, virus, attempted fraud
- Leverage GAMP's classic three-components risk assessment
  - Degree of harm
  - Probability of fault
  - Detectability of fault

Simple Risk Assessment

- GAMP 4 describes a simple two-step process
  1. Plot **severity** vs. **probability** to obtain **risk class**
  2. Plot **risk class** vs. **detectability** to obtain ***risk priority***



ISO 14971-Based Approach to Risk



Controls Based on Risk and Impact

Effect on:
Patient safety
Product safety
Compliance

Direct Impact:
Use risk assessment to identify specific controls & rigor

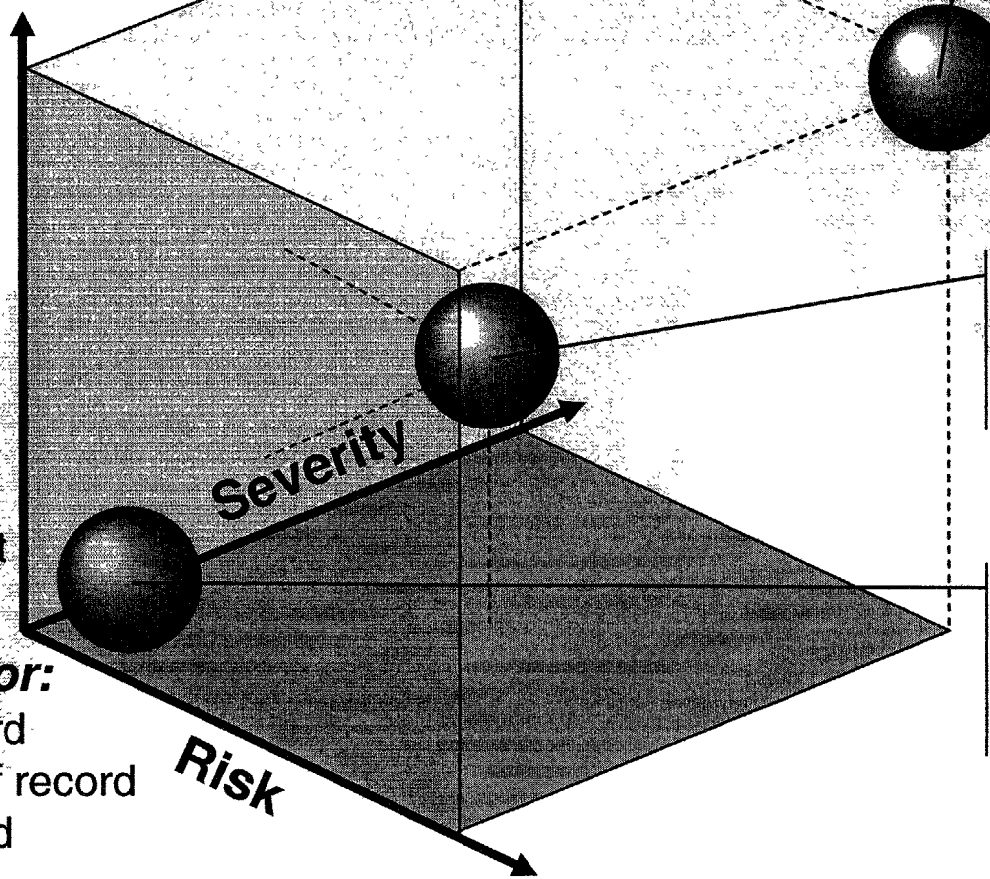
Indirect Impact:
Use Generic Checklist controls

No Impact:
Use "Good IT Practices"

Increasing rigor of control required

Consider:

Stricter controls
More controls
More frequent controls
Automatic controls
Increased internal audit



Potential for:
Loss of record
Corruption of record
Wrong record

Controls Based on Risk and Impact

Control	No Impact "Good IT Practice"	Indirect Impact Formal Processes for:	Direct Impact Formal processes for:
Access control	- Controlled access	• authorization process • access management • password management • documentation	• rigorous authorization control • strict and proactive access management • user profiles • unique accounts • stringent PW management • physical security • full documentation
Backup and Restore	• Checking of outcome • Multiple copies (redundancy)	• Checking of outcome • Multiple copies (redundancy) • Formal periodic testing • Documentation	• Checking of outcome • Multiple copies (redundancy) • Formal periodic testing • Full documentation • Remote storage locations • Automated processes

Rigor of Controls

Appendices

- Validation Policy
  - Validation is an expected control
- Audit Trails and Data Security
  - Level of control commensurate with risk/impact
  - Audit trails only where they make sense
- Record retention
  - Format choice reflects actual business process
  - Format choices based on risk assessment
  - Optimal format may change as record ages

Appendices

- Copies of Records
  - Useful access necessary for inspectors
  - Use of common portable formats
- Legacy Systems
  - Document justification of classification as legacy
    - Guidelines for evaluating effect of upgrades
  - Document that system satisfies predicate rule
- Predicate Rules Requiring Records or Signatures
  - US (21 CFR 50, 54, 56, 58, 210, 211, 312, 314, 820)
  - EU
  - Japan

Appendices

- Sample Case Studies
  - Spreadsheets
  - Packaging equipment
  - Clinical trial label manufacture
  - SCADA
  - HPLC
  - Chromatography Data System
  - Interactive Voice Response System (IVRS)
  - Adverse Event Reporting System
  - Batch record system

Appendices

- Forms for Indirect Impact Records
  - For risk assessment and identification of controls
- Risk Assessment for Direct Impact Electronic Records
  - Adapted from GAMP 4 Appendix M3
  - Includes roles and responsibilities
- Form for Previously Assessed Part 11 Systems
- Glossary
- References

Summary

- The New GAMP GPG for Electronic Record and Signature Compliance offers
  - A pragmatic approach to complying with record requirements in electronic systems
  - A combination of record classification and risk assessment that
    - Places controls where they are needed
    - Is not so ponderous that firms will find it easier to work toward a single excessive standard
  - Extensive examples of application of the process